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| 10/565,417 | 08/03/2006 | William J. Welsh | UMD0067US.NP | 2667 |
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| LICATA & TYRRELL P.C. 66 EAST MAIN STREET MARLTON, NJ 08053 | | | EXAMINER SMITH, CAROLYN L | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/565,417 | Applicant(s) WELSH ET AL. | |
| | Examiner Carolyn L. Smith | Art Unit 1631 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>02162006</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to systems and methods for microarray data analysis, whereas in contrast the claims are specifically directed to a method, computer program product, computer software program, and a computer for imputing missing values in microarray analysis.

The drawing, filed 1/23/06, is accepted by the Examiner.

Claims herein under examination are 1-8.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 24, line 10. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Under the Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility (published in the O.G. notice (1300 OG 142) on 11/22/2005) a method that does not result in a physical transformation of matter MAY be statutory where it recites a concrete, tangible and useful result; i.e. a practical application.

Claims 1-6 are drawn to a method, computer program product, and a computer software program. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the claims 1-6, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result. In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be “useful,” the claim must produce a result that is specific, and substantial. For a claim to be “concrete,” the process must have a result that is reproducible. For a claim to be “tangible,” the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

In the instant case, claims 1-6 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. The method as claimed is drawn to computational means for imputing missing values in microarray data. However, as claimed, the method does not include a real world result. For example, method as claimed may take entirely within the confines of a computer or human mind without any

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communication to the outside world. A tangible requirement requires that the claim must set forth a practical application of the computational steps to produce a real-world result. No practical result is recited in these claims; thus the instant claims do not include any tangible result.

Regarding computer program products and computer software programs, Applicants are directed to the following passage in MPEP 2106.01:

Data structures not claimed as embodied in computer-readable media are descriptive material per se and are not statutory because they are not capable of causing functional change in the computer. See, e.g., *Warmerdam*, 33 F.3d at 1361, 31 USPQ2d at 1760 (claim to a data structure per se held nonstatutory). Such claimed data structures do not define any structural and functional interrelationships between the data structure and other claimed aspects of the invention which permit the data structure's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a data structure defines structural and functional interrelationships between the data structure and the computer software and hardware components which permit the data structure's functionality to be realized, and is thus statutory.

Similarly, computer programs claimed as computer listings per se, i.e., the descriptions or expressions of the programs, are not physical "things." They are neither computer components nor statutory processes, as they are not "acts" being performed. Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory. See *Lowry*, 32 F.3d at 1583-84, 32 USPQ2d at 1035. Accordingly, it is important to distinguish claims that define descriptive material per se from claims that define statutory inventions.

The rejection for the method claims could be overcome by amending these claims to recite that a result of the method is outputted to a display or a memory, or by including a physical transformation (provided there is adequate written support in the originally filed application).

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1, 2, 4, 6 and 8 are vague and indefinite due to the unclarity of citing an abbreviation, such as "GMCimpute" and "K". It is unclear what these abbreviations are intended to mean. Correction is suggested by amending in of the full name in parentheses. Claims 3, 5, and 7 are also rejected due to their dependency from claim 1.

Claims 2 (line 4), 4 (line 4), 6 (line 4), and 8 (line 4) recite the limitation "the rows". There is insufficient antecedent basis for this limitation in these claims as there is no previous mention of any rows. Clarification of this issue via clearer claim wording is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Troyanskaya et al. (Bioinformatics, 2001, Volume 17, Number 6, pages 520-525) with additional support from online Merriam-Webster dictionary ("Gaussian" definition).

Troyanskaya et al. disclose methods for estimating missing values in DNA microarrays via imputing (abstract and title). Troyanskaya et al. disclose k-means clustering and various model-based approaches and algorithms, such as (Single Value Decomposition) SVDimpute algorithm via normalization (page 520, col. 2, first column; page 521, col. 1, first and second and fourth paragraphs and col. 2, first and last paragraph). According to the online Merriam-Webster dictionary, the definition of "Gaussian" is "being or having the shape of a normal curve or a normal distribution" (this definition is not being used as prior art, but rather to clarify the definition of the term "Gaussian"). The normalization of data represents normal distributions or Gaussian distributions or models. Troyanskaya et al. disclose using k eigengenes, using a row average, and an expectation maximization method that is repeated until the change falls below a threshold (converges) (page 522, col. 1, third and fourth paragraphs). Troyanskaya et al. disclose software and methods implemented on a computer (abstract and page 524, col. 1, last paragraph) which represents a computer program product and program and computer which inherently contains memory.

Thus, Troyanskaya et al. with additional support from online Merriam-Webster dictionary anticipate the instant invention.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Hytopoulos et al. (US 2002/0169560 A1) with additional support from online Merriam-Webster dictionary (“Gaussian” definition).

Hytopoulos et al. disclose a computer-implemented method and a system using microarray expression data arrays, cluster arrays, and clustering tools wherein the expression values have been normalized, filtered, and imputed, wherein missing data are imputed (abstract and paragraphs 0002, 0052 and 0123). According to the online Merriam-Webster dictionary, the definition of “Gaussian” is “being or having the shape of a normal curve or a normal distribution” (this definition is not being used as prior art, but rather to clarify the definition of the term “Gaussian”). The normalization of data represents normal distributions or Gaussian distributions or models. Hytopoulos et al. disclose using a computer readable medium in association with a computer including a processor and memory and computer instructions which are configured to cause a computer to process data (claim 15) which represents an algorithm and computer software program and product. Hytopoulos et al. disclose allowing the user to select K-nearest neighbor imputation mechanism or other data imputation mechanisms (paragraph 0125). Hytopoulos et al. disclose analysis of gene expression data to form clusters (abstract). Hytopoulos et al. disclose identifying genes represented in respective rows (paragraph 0038)

which represents a partitioning of rows of microarray data. Hytopoulos et al. disclose mapping rows of expression data (paragraph 0131). Thus, Hytopoulos et al. with additional support from online Merriam-Webster dictionary anticipate claims 1, 3, 5, and 7.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 4, 6, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hytopoulos et al. (US2002/0169560 A1) with additional support from online Merriam-Webster dictionary (“Gaussian” definition) as applied to claims 1, 3, 5, and 7 above, and further in view of Cereghini et al. (US 6,496,834 B1).

Hytopoulos et al. describe the limitations in instant claims 1, 3, 5, and 7, as discussed

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above in the 35 USC 102 rejection. Hytopoulos et al. do not describe repeating a classification expectation-maximization algorithm until the K partitions converge.

Cereghini et al. describe a method of performing cluster analysis inside a relational database management system using Gaussian mixture parameters and implementing an Expectation-Maximization (EM) clustering algorithm iteratively (abstract). Cereghini et al. describe grouping a set of data into k clusters with k rows (partitioned) (col. 2, lines 57-63). Cereghini et al. describe the expectation-maximization algorithm converges quickly and performing iterations (col. 9, lines 34-42).

Hytopoulos et al. state that effective mechanisms for analyzing DNA array data are needed to determine which genes or combination of genes are correlated to various human conditions (paragraph 0009). Cereghini et al. state the EM algorithm is robust for noisy data and missing information (col. 7, lines 5-6). Cereghini et al. state cluster analysis does not typically work well with large databases due to memory limitations and the execution times required (col. 2, lines 32-39). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use effective means for analyzing DNA array data, as stated by Hytopoulos et al., by using algorithms supporting large databases, as stated by Cereghini et al. The person of ordinary skill in the art would have been motivated to make that modification in order to find effective ways (as stated by Hytopoulos et al. and Cereghini et al.) of correlating genes to human conditions (as stated by Hytopoulos et al.) by allowing non-statisticians to benefit from advanced mathematical techniques available in a relational environment, as stated by Cereghini et al. (col. 2, lines 40-43).

Thus, Hytopoulos et al. with additional support from the online Merriam-Webster

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dictionary, in view of Cereghini et al. motivate the instant invention.

Conclusion


No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

April 19, 2007


Carolyn Smith
Examiner
AU 1631